That which is claimed is:

1. A method for identifying a compound having the ability to modulate virus propagation in a host cell comprising the steps of:

(a) generating a three-dimensional model of a protein required for viability of a virus, or a portion thereof;

(b) generating a three-dimensional model of a potential modulator compound of interest; and

(c) determining at least one atomic interaction between the potential modulator compound and the protein, or a portion thereof, as defined by the three-dimensional models of (a) and (b).

2. The method of claim 1, wherein the virus is an orthopox virus.

3. The method of claim 2, wherein the protein is the vaccinia virus I7L protein.

4. The method of claim 1, wherein steps (a) (b) and (c) further comprise:

(a) generating a three-dimensional computer model of the protein, or a portion thereof;

(b) generating a three-dimensional computer model of the potential modulator compound of interest;

(c1) using a computer to dock the three-dimensional model of the potential modulator compound with the model of the protein or a portion thereof; and

(c2) quantifying at least one atomic interaction between the potential modulator compound and the protein, or a portion thereof.

5. The method of claim 4, further comprising:

(d) modifying the computer model of the potential modulator compound of interest; and

(e) evaluating how modifying the computer model of the potential modulator compound changes at least one atomic interaction between of the model of the potential modulator compound and the model of the protein, or portion thereof.

6. The method of claim 5, wherein the step of modifying the computer model of the potential modulator compound comprises:

(i) searching a library of molecular structures for molecular fragments that can be linked to the potential modulator compound, wherein a molecular fragment comprises at least one atom; and

(ii) linking a fragment to the potential modulator compound to generate a modified computer model of the compound.

7. Compounds identified by the method of claim 1.

8. A method for identifying a compound having the ability to modulate orthopox virus propagation in a host cell comprising the steps of:

(a) generating a three-dimensional model of an I7L protein, or a portion thereof,

(b) generating a three-dimensional model of a potential modulator compound of interest; and

(c) determining at least one atomic interaction between the potential modulator compound and the I7L, or a portion thereof, as defined by the three-dimensional models of (a) and (b).

9. The method of claim 8, wherein the model of I7L protein, or a portion thereof, comprises the atomic coordinates as defined in Table 2.

10. The method of claim 8, wherein the method of generating the computer model comprises aligning the structure of the I7L protein, or a portion thereof, with a second cysteine protease, or a portion thereof.

11. The method of claim 10, wherein the second cysteine protease is ubiquitin-like protein 1 (ULP1) protease, or a portion thereof.

12. The method of claim 11, wherein the amino acids used to align the structure of the I7L protein, or a portion thereof, with the ULP1, or a portion thereof, comprise His241, Asp248, and Cys328 of the I7L protein and His514, Cys580 and Trp448 of ULP1.

13. The method of claim 8, wherein steps (a), (b) and (c) further comprise:

(a) generating a three-dimensional computer model of the I7L protein, or a portion thereof;

(b) generating a three-dimensional computer model of the potential modulator compound;

(c1) using a computer to dock the three-dimensional model of the potential modulator compound with the model of the I7L protein, or a portion thereof; and

(c2) quantifying at least one atomic interaction between the potential modulator compound and the I7L protein, or a portion thereof.

14. The method of claim 13, further comprising the steps of:

(d) modifying the computer model of the potential modulator compound; and

(e) evaluating how modifying the computer model of the potential modulator compound changes the atomic interactions between of the model of the potential modulator compound and the model of the I7L protein, or portion thereof.

15. The method of claim 14, wherein the step of modifying the computer model of the potential modulator compound comprises:

(i) searching a library of molecular structures for molecular fragments that can be linked to the potential modulator compound, wherein a molecular fragment comprises at least one atom; and

(ii) linking a fragment to the potential modulator compound to generate a modified computer model of the compound.

16. The method of claim 8, wherein the I7L protein, or a portion thereof, comprises a ligand binding domain.

17. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises an atomic interaction between the compound and the catalytic cysteine.

18. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of amino acids Cys328, His241, Asp248, or Asp258 of the I7L protein.

19. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of Leu324, Trp242, Gln322, Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203,or Met233 of the I7L protein.

20. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises Cys(N), wherein position N corresponds to the catalytic cysteine of the I7L.

21 The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of His(N-87), Asp(N-80), or Asp(N-70), wherein position N corresponds to the catalytic cysteine of the I7L.

22. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of Trp(N-86), Gln(N-6), Leu(N-4), Gly(N+1), Leu(N-

5), Ser(N-88), Trp(N-160), Asp(N-134), Asn(N-157), Ser(N-155), Met(N-133), Ser(N-2), Glu(N-1), Leu(N-89), Leu(N-151), Asn(N-129), Met(N-159), Phe(N-92), Ile(N-125), or Met(N-95),wherein position N corresponds to the catalytic cysteine of the I7L.

23. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of a wild-type or altered amino acid in the I7L protein corresponding to positions 168, 169, 171, 173, 177, 194, 195, 199, 203, 233, 236, 239, 240, 241, 242, 248, 258, 322, 323, 324, 326, 327, 328, or 329 of the wild-type I7L protein.

24. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic.

25. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, comprises at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

26. The method of claim 8, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

27. The method of claim 8, wherein the potential modulator compound is evaluated for its interaction with a modified I7L protein, or portion thereof, comprising amino acid substitutions, deletions and insertions of the I7L.

28. The method of claim 8, wherein the orthopox virus comprises smallpox virus, vaccinia virus, monkeypox virus, mulluscipox virus, cowpox virus, camelpox virus, variola major virus, variola minor virus, ectromelia virus, sheeppox virus, lumpy skin virus, Yaba-like virus, swinepox virus, rabbit fibroma virus, myxoma virus, fowlpox virus, or canarypox virus.

29. Compounds identified by the method of claim 8.

30. A method of generating a three-dimensional model of a protein, or a portion thereof, comprising the steps of: (a) providing an amino acid sequence of a protein of interest; (b) comparing the amino acid sequence of the protein of interest to the amino acid sequences for a plurality of other proteins; (c) identifying a second protein for which a three-dimensional structure has been defined, and that has a predetermined level of sequence identity to the protein of interest; (d) aligning conserved residues from the protein of interest with conserved

residues from the second protein; and (e) threading the protein of interest along the three-dimensional structure of the second protein such that the position of at least two conserved residues from both proteins are aligned.

31. The method of claim 30, wherein the conserved residues from the protein of interest and the second protein comprise residues that are essential for protein function.

32. The method of claim 30, wherein the second protein aligned with the protein of interest comprises a protein having a similar function to the protein of interest.

33. The method of claim 30, wherein the protein of interest comprises vaccinia virus I7L and the second protein comprises ubiquitin-like protein 1 (ULP1).

34. The method of claim 33, wherein the amino acids used to align the structure of the I7L protein, or a portion therof, with ULP1 protein, or a portion threof, comprise His241, Asp248, and Cys328 of the I7L protein and His 514, Cys 580 and Trp448 of ULP1.

35. A computer model for I7L protein, or a portion thereof, comprising atomic coordinates for a three-dimensional model for I7L protein, or a portion thereof, operable to be visualizable on a computer screen.

36. The computer model of claim 35, wherein the atomic coordinates for I7L, or a portion thereof, comprise at least some of the atomic coordinates as defined in Table 2.

37. The computer model of claim 35, further comprising a three-dimensional computer model of a potential modulator compound docked with the I7L structure such that at least one atomic interaction between the I7L protein and the potential modulator compound may be quantified.

38. The computer model of claim 37, wherein the atomic interaction between the I7L and the potential modulator compound are defined at least in part determining the atomic coordinates for the potential modulator compound as the compound interacts with the I7L protein.

39. The computer model of claim 37, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises an atomic interaction between the compound and the catalytic cysteine of the I7L protein, wherein the atomic interaction is selected from the group consisting of charge and electrostatic.

40. The computer model of claim 37, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of amino acids Cys3328, His241, or Asp248, Asp258, of the I7L protein.

41. The computer model of claim 37, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction between the compound and at least one of amino acids Leu324, Trp242, Gln322, Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein.

42. The computer model of claim 37, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic.

43. The computer model of claim 37, wherein the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, comprises at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

44. The computer model of claim 37, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

45. A pharmacophore comprising at least one atom that interacts with at least one atom of an I7L protein, or a portion thereof.

46. The pharmacophore of claim 45, wherein the three dimensional structure of the pharmacophore comprises at least one atom that interacts with the I7L ligand binding domain, or a portion thereof.

47. The pharmacophore of claim 45, wherein the three-dimensional structure of I7L comprises at least some of the atomic coordinates as defined in Table 2.

48. The pharmacophore of claim 45, wherein the spatial arrangement of atoms within the pharmacophore comprise at least some of the atomic coordinates of at least one docking mode as defined in Table 3.

49. The pharmacophore of claim 45, wherein the spatial arrangement of atoms within the pharmacophore comprises at least some of the atomic coordinates of at least one docking mode as defined in Table 4.

50. The pharmacophore of claim 45, wherein the at least one atom of I7L that interacts with the pharmacophore comprises the catalytic cysteine of I7L, and wherein the atomic interaction is selected from the group consisting of charge and electrostatic.

51. The pharmacophore of claim 45, wherein the at least one atom of I7L that interacts with the pharmacophore comprises at least one of Cys328, His241, Asp248, Asp258, Leu324, Trp242, Gln322, Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein.

52. The pharmacophore of claim 45, wherein the atomic interaction between the pharmacophore and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic.

53. The pharmacophore of claim 45, wherein the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, comprises at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

54. The pharmacophore of claim 45, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

55. A compound comprising at least one atom that that interacts with at least one atom of an I7L protein, or a portion thereof, to modulate the activity of I7L.

56. The compound of claim 55, wherein the compound interacts with the ligand binding domain of I7L.

57. The compound of claim 55, wherein the interaction between the compound and I7L protein, or a portion thereof, comprises an *in silico* interaction defined by docking a computer model of the structure of the compound with a computer model of the I7L protein, or a portion thereof.

58. The compound of claim 55, wherein the structure of I7L protein, or a portion thereof is defined by at least some of the atomic coordinates in Table 2.

59. The compound of claim 55, wherein the spatial arrangement of atoms within the compound comprises at least some of the atomic coordinates of at least one docking mode as defined in Table 3.

60. The compound of claim 55, wherein the spatial arrangement of atoms within the compound comprises at least some of the atomic coordinates of at least one docking mode as defined in Table 4.

61. The compound of claim 55, wherein the compound interacts with the ligand binding domain of I7L.

62. The compound of claim 55, wherein the at least one atom of I7L that interacts with the compound comprises the catalytic cysteine of I7L.

63. The compound of claim 55, wherein the at least one atom of I7L that interacts with the pharmacophore comprises at least one of Cys328, His241, Asp248, Asp258, Leu324, Trp242, Gln322, Gly329, Leu323, Ser240, Trp168, Asp194, Asn171, Ser173, Gln 322, Met195, Ser326, Glu327, Leu239, Leu177, Asn199, Met169, Phe236, Ile203, or Met233 of the I7L protein.

64. The compound of claim 55, wherein the interaction between the compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic.

65. The compound of claim 55, wherein the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, comprises at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

66. The compound of claim 55, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

67. A pharmaceutical composition comprising a compound identified by docking a computer representation of the compound with a computer representation of a structure of I7L protein, or a portion thereof.

68. The pharmaceutical composition of claim 67, wherein the structure of I7L, or a portion thereof, comprises at least some of the atomic coordinates as defined by Table 2.

69. The pharmaceutical composition of claim 67, wherein the spatial arrangement of atoms within the compound comprises at least some of the atomic coordinates of at least one docking mode as defined in Table 3.

70. The pharmaceutical composition of claim 67, wherein the spatial arrangement of atoms within the compound comprises at least some of the atomic coordinates of at least one docking mode as defined in Table 4.

71. The pharmaceutical composition of claim 67, wherein the interaction between the compound and the I7L protein, or a portion thereof, comprises at least one atomic interaction selected from the group consisting of charge, electrostatic, hydrogen bond, and hydrophobic.

72. The pharmaceutical composition of claim 67, wherein the atomic interaction between a potential modulator compound and the I7L protein, or portion thereof, comprises at least two hydrogen bond atomic interactions, at least two hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

73. The pharmaceutical composition of claim 67, wherein the atomic interaction between a potential modulator compound and the I7L protein, or a portion thereof, comprises at least three hydrogen bond atomic interactions, at least three hydrophobic atomic interactions, and at least one of a charge or electrostatic interaction.

74. The pharmaceutical composition of claim 67, wherein the compound is present in a therapeutically effective amount, wherein a therapeutically effective amount comprises an amount sufficient to reduce a viral load in a subject.

75. The pharmaceutical composition of claim 74, wherein a therapeutically effective amount comprises as a dose in a range from about 0.01 to 1,000 mg of active compound per kg body weight per day.

76. The pharmaceutical composition of claim 74, wherein the viral load comprises an orthopox virus.

77. The pharmaceutical composition of claim 76, wherein the orthopox virus comprises smallpox virrus, vaccinia virus, monkeypox virus, mulluscipox virus, cowpox virus, camelpox virus, variola major virus, variola minor virus, ectromelia virus, sheeppox virus, lumpy skin virus, Yaba-like virus, swinepox virus, rabbit fibroma virus, myxoma virus, fowlpox virus, or canarypox virus.

78. The pharmaceutical composition of claim 67, further comprising one or more additional antiviral agents.

79. A method of conducting a drug discovery business comprising:

(a) generating a three-dimensional structural model of a target molecule of interest on a computer;

(b) generating a three-dimensional structural model of a potential modulator compound of the target molecule of interest on a computer; and

(c) docking the model for the potential modulator compound with the target molecule of interest so as to minimize the free energy of the interaction between the target molecule and the potential modulator.

80. The method of claim 79, further comprising the steps of:

(d) providing a modified structure for the modulator compound of interest; and

(e) assessing whether the modified structure has a lower free energy of interaction with the target of interest.

81. A method of treating orthopox infections comprising administering a therapeutically effective amount of a compound identified by the steps of:

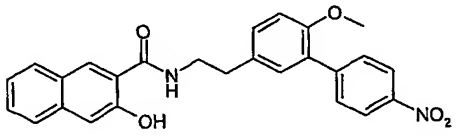
(a) generating a three-dimensional model of a I7L protein, or a portion thereof,

(b) generating a three-dimensional model of a potential modulator compound of interest; and

(c) determining the atomic interactions between the potential modulator compound and the I7L protein, or a portion thereof, as defined by the three-dimensional models of (a) and (b).

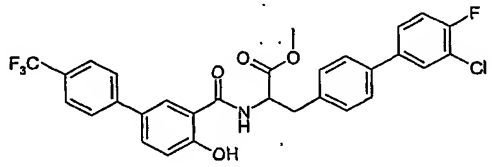
82. The method of claim 81, wherein the compound comprises a small organic compound.

83. The method of claim 82, wherein the compound comprises TTP-A,



or a salt or prodrug thereof.

84. The method of claim 82, wherein the compound comprise TTP-B,



or a salt or prodrug thereof.